Prospective Detection of Preclinical Lung Cancer: Results from Two Studies of Heterogeneous Nuclear Ribonucleoprotein A2/B1 Overexpression

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Abstract: The United States lung cancer epidemic has not yet been controlled by present prevention and treatment strategies. Overexpression of a M_r 31,000 protein, heterogeneous nuclear ribonucleoprotein (hnRNP) A2/B2, had shown promise as a marker of lung cancer. In a pilot study of archived preneoplastic sputum specimens, hnRNP A2/B1 overexpression more accurately detected preclinical lung cancer than standard cytomorphology. In separate, ongoing prospective studies, sputum is collected annually from stage I resected non-small cell lung cancer patients at high risk of developing a second primary lung cancer and Yunnan tin miners at high risk of primary lung cancer. After the first year of follow-up, preclinical detection of lung cancer by routine cytology was compared with hnRNP A2/BI overexpression as measured by quantitative densitometry of immunostained slides. Up-regulation of hnRNP A2/B1 in sputum specimens accurately predicted the outcome in 32 of 40 primary lung cancer and control patients within 12 months, whereas cytological change suggestive of lung cancer was found in only 1 patient. In the primary lung cancer study, overexpreesed hnRNP A2/B1 accurately predicted the outcome in 69 of 94 primary lung cancer and control miners, whereas only 10 with primary lung cancer were diagnosed cytologically. These two prospective studies accurately predicted that 67 and 69% of those with hnRNP A2/B1 up-regulation in their sputum would develop lung cancer in the first year of follow-up, compared with background lung cancer risks of 2.2 and 0.9% (35 and 76-fold increase, respectively). Using sputum cells to monitor hnRNP A2/B1 expression may greatly improve the accuracy of preclinical lung cancer detection.